ORC1 gene

origin recognition complex subunit 1

Normal Function

The *ORC1* gene provides instructions for making a protein that is important in the copying of a cell's DNA before the cell divides (a process known as DNA replication). The protein produced from this gene is one of a group of proteins known as the origin recognition complex (ORC). (The complex is made up of the proteins ORC1 to ORC6, which are produced from different genes.) ORC attaches (binds) to certain regions of DNA known as origins of replication (or origins), where the process of DNA copying begins. This complex attracts additional proteins to bind to it, forming a larger group of proteins called the pre-replication complex. When the pre-replication complex is attached to the origin, replication is able to begin at that location. This tightly controlled process, called replication licensing, helps ensure that DNA replication occurs only once per cell division and is required for cells to divide.

ORC also attaches to a form of DNA called heterochromatin. Heterochromatin is densely packed DNA that contains few functional genes, but it is important for controlling gene activity and maintaining the structure of chromosomes. It is unclear what effect ORC binding has on heterochromatin.

In addition to its roles as part of ORC, the ORC1 protein is involved in the copying of cell structures called centrosomes and centrioles, which are important for the process of cell division. ORC1 blocks centrosomes and centrioles from being copied more than once, which is key to normal cell division. In addition, some research suggests that ORC1 is involved in the function of cilia, which are microscopic, finger-like projections that stick out from the surface of cells. Cilia participate in signaling pathways that transmit information within and between cells and are important for the development and function of many types of cells and tissues, including bone.

Health Conditions Related to Genetic Changes

Meier-Gorlin syndrome

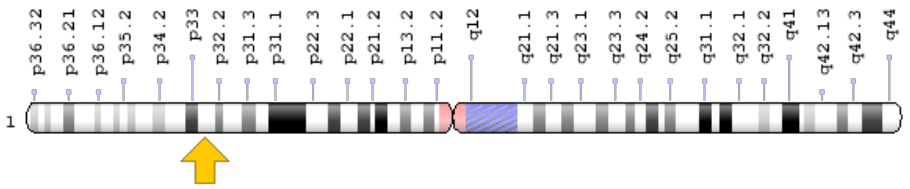
Mutations in the *ORC1* gene cause Meier-Gorlin syndrome, a condition characterized by short stature, underdeveloped kneecaps, and small ears. These mutations alter the ORC1 protein, typically by changing single protein building blocks (amino acids) or by leading to production of an abnormally short version of the ORC1 protein. As a result, assembly of the pre-replication complex is impaired, which disrupts replication licensing; however, it is not clear how a reduction in replication licensing leads to Meier-Gorlin syndrome. Researchers speculate that such a reduction delays the

cell division process, which slows growth of the bones and other tissues during development and may contribute to the features of the disorder. Some studies suggest that alterations of ORC1 result in too many copies of centrosomes and centrioles, which may also delay cell division. Other studies suggest that changes in ORC1 impair the function of cilia, which may delay development of certain tissues and underlie the abnormal development of kneecaps and ears characteristic of Meier-Gorlin syndrome.

Chromosomal Location

Cytogenetic Location: 1p32.3, which is the short (p) arm of chromosome 1 at position 32.3

Molecular Location: base pairs 52,371,408 to 52,404,471 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- HSORC1
- ORC1_HUMAN
- ORC1L
- origin recognition complex, subunit 1
- origin recognition complex, subunit 1 homolog
- PARC1
- replication control protein 1

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): DNA Synthesis Begins at Replication Origins
  https://www.ncbi.nlm.nih.gov/books/NBK26826/#_A796_
- The Cell: A Molecular Approach (second edition, 2000): Origins and the Initiation of Replication
  https://www.ncbi.nlm.nih.gov/books/NBK9940/#_A789_

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28ORC1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- ORIGIN RECOGNITION COMPLEX, SUBUNIT 1, S. CEREVISIAE, HOMOLOG OF
  http://omim.org/entry/601902

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ORC1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ORC1%5Bgene%5D
- HGNC Gene Family: AAA ATPases
  http://www.genenames.org/cgi-bin/genefamilies/set/413
- HGNC Gene Family: Origin recognition complex
  http://www.genenames.org/cgi-bin/genefamilies/set/960
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=8487
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4998
- UniProt
  http://www.uniprot.org/uniprot/Q13415

Sources for This Summary

- Bicknell LS, Bongers EM, Leitch A, Brown S, Schoots J, Harley ME, Aftimos S, Al-Aama JY, Bober M, Brown PA, van Bokhoven H, Dean J, Edrees AY, Feingold M, Fryer A, Hoefsloot LH, Kau N, Knoers NV, Mackenzie J, Opitz JM, Sarda P, Ross A, Temple IK, Toutain A, Wise CA, Wright M, Jackson AP. Mutations in the pre-replication complex cause Meier-Gorlin syndrome. Nat Genet. 2011 Feb 27;43(4):356-9. doi: 10.1038/ng.775.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21358632
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3068194/
- Bicknell LS, Walker S, Klingseisen A, Stiff T, Leitch A, Kerzendorfer C, Martin CA, Yeyati P, Al Sanna N, Bober M, Johnson D, Wise C, Jackson AP, O'Driscoll M, Jeggo PA. Mutations in ORC1, encoding the largest subunit of the origin recognition complex, cause microcephalic primordial dwarfism resembling Meier-Gorlin syndrome. Nat Genet. 2011 Feb 27;43(4):350-5. doi: 10.1038/ng.776.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21358633
- Hemerly AS, Prasanth SG, Siddiqui K, Stillman B. Orc1 controls centriole and centrosome copy number in human cells. Science. 2009 Feb 6;323(5915):789-93. doi: 10.1126/science.1166745.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19197067
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2653626/
- Hossain M, Stillman B. Meier-Gorlin syndrome mutations disrupt an Orc1 CDK inhibitory domain and cause centrosome reduplication. Genes Dev. 2012 Aug 15;26(16):1797-810. doi: 10.1101/gad.197178.112. Epub 2012 Aug 1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22855792
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3426759/
- Niida H, Kitagawa M. Regulation of DNA replication licensing. Curr Drug Targets. 2012 Dec;13(13):1588-92. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22998185
- OMIM: ORIGIN RECOGNITION COMPLEX, SUBUNIT 1, S. CEREVISIAE, HOMOLOG OF http://omim.org/entry/601902
- Prasanth SG, Shen Z, Prasanth KV, Stillman B. Human origin recognition complex is essential for HP1 binding to chromatin and heterochromatin organization. Proc Natl Acad Sci U S A. 2010 Aug 24;107(34):15093-8. doi: 10.1073/pnas.1009945107. Epub 2010 Aug 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20689044
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2930523/

- Stiff T, Alagoz M, Alcantara D, Outwin E, Brunner HG, Bongers EM, O'Driscoll M, Jeggo PA. Deficiency in origin licensing proteins impairs cilia formation: implications for the aetiology of Meier-Gorlin syndrome. PLoS Genet. 2013;9(3):e1003360. doi: 10.1371/journal.pgen.1003360. Epub 2013 Mar 14.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23516378
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3597520/
- de Munnik SA, Bicknell LS, Aftimos S, Al-Aama JY, van Bever Y, Bober MB, Clayton-Smith J, Edrees AY, Feingold M, Fryer A, van Hagen JM, Hennekam RC, Jansweijer MC, Johnson D, Kant SG, Opitz JM, Ramadevi AR, Reardon W, Ross A, Sarda P, Schrander-Stumpel CT, Schoots J, Temple IK, Terhal PA, Toutain A, Wise CA, Wright M, Skidmore DL, Samuels ME, Hoefsloot LH, Knoers NV, Brunner HG, Jackson AP, Bongers EM. Meier-Gorlin syndrome genotype-phenotype studies: 35 individuals with pre-replication complex gene mutations and 10 without molecular diagnosis. Eur J Hum Genet. 2012 Jun;20(6):598-606. doi: 10.1038/ejhg.2011.269. Epub 2012 Feb 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22333897
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3355263/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/ORC1

Reviewed: February 2014
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services